SEQUENCE LISTING

<110> Allison, Anthony

<120> MODIFIED ANNEXIN PROTEINS AND METHODS FOR TREATING VASO-OCCLUSIVE
       SICKLE-CELL DISEASE

<130> SURR.113

<150> 60/400,718
<151> 2002-08-02

<150> 10/080,370
<151> 2002-02-21

<160> 9

<170> PatentIn version 3.2

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<213> Homo sapiens

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ggcagggatc ttctggatga cctgaaatca gaactaactg gaaaatttga aaaattaatt   240

gtggctctga tgaaaccctc tcggctttat gatgcttatg aactgaaaca tgccttgaag   300

ggagctggaa caaatgaaaa agtactgaca gaaattattg cttcaaggac acctgaagaa   360

ctgagagcca tcaaacaagt ttatgaagaa gaatatggct caagcctgga agatgacgtg   420

gtgggggaca cttcagggta ctaccagcgg atgttggtgg ttctccttca ggctaacaga   480

gaccctgatg ctggaattga tgaagctcaa gttgaacaag atgctcaggc tttatttcag   540

gctggagaac ttaaatgggg gacagatgaa gaaaagttta tcaccatctt tggaacacga   600

agtgtgtctc atttgagaaa ggtgtttgac aagtacatga ctatatcagg atttcaaatt   660

gaggaaacca ttgaccgcga gacttctggc aatttagagc aactactcct tgctgttgtg   720

aaatctattc gaagtatacc tgcctacctt gcagagaccc tctattatgc tatgaaggga   780

gctgggacag atgatcatac cctcatcaga gtcatggttt ccaggagtga gattgatctg   840

tttaacatca ggaaggagtt taggaagaat tttgccacct ctctttattc catgattaag   900

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Ala Gln Val Leu Arg Gly Thr Val Thr Asp Phe Pro Gly Phe Asp Glu
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cgg gct gat gca gaa act ctt cgg aag gct atg aaa ggc ttg ggc aca      96
Arg Ala Asp Ala Glu Thr Leu Arg Lys Ala Met Lys Gly Leu Gly Thr
            20                  25                  30

gat gag gag agc atc ctg act ctg ttg aca tcc cga agt aat gct cag     144
Asp Glu Glu Ser Ile Leu Thr Leu Leu Thr Ser Arg Ser Asn Ala Gln
        35                  40                  45

cgc cag gaa atc tct gca gct ttt aag act ctg ttt ggc agg gat ctt     192
Arg Gln Glu Ile Ser Ala Ala Phe Lys Thr Leu Phe Gly Arg Asp Leu
    50                  55                  60

ctg gat gac ctg aaa tca gaa cta act gga aaa ttt gaa aaa tta att     240
Leu Asp Asp Leu Lys Ser Glu Leu Thr Gly Lys Phe Glu Lys Leu Ile
65                  70                  75                  80

gtg gct ctg atg aaa ccc tct cgg ctt tat gat gct tat gaa ctg aaa     288
Val Ala Leu Met Lys Pro Ser Arg Leu Tyr Asp Ala Tyr Glu Leu Lys
                85                  90                  95

cat gcc ttg aag gga gct gga aca aat gaa aaa gta ctg aca gaa att     336
His Ala Leu Lys Gly Ala Gly Thr Asn Glu Lys Val Leu Thr Glu Ile
                100                 105                 110

att gct tca agg aca cct gaa gaa ctg aga gcc atc aaa caa gtt tat     384
Ile Ala Ser Arg Thr Pro Glu Glu Leu Arg Ala Ile Lys Gln Val Tyr
            115                 120                 125

gaa gaa gaa tat ggc tca agc ctg gaa gat gac gtg gtg ggg gac act     432
Glu Glu Glu Tyr Gly Ser Ser Leu Glu Asp Asp Val Val Gly Asp Thr
        130                 135                 140

tca ggg tac tac cag cgg atg ttg gtg gtt ctc ctt cag gct aac aga     480
Ser Gly Tyr Tyr Gln Arg Met Leu Val Val Leu Leu Gln Ala Asn Arg
145                 150                 155                 160

gac cct gat gct gga att gat gaa gct caa gtt gaa caa gat gct cag     528
Asp Pro Asp Ala Gly Ile Asp Glu Ala Gln Val Glu Gln Asp Ala Gln
                165                 170                 175
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2

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gct tta ttt cag gct gga gaa ctt aaa tgg ggg aca gat gaa gaa aag        576
Ala Leu Phe Gln Ala Gly Glu Leu Lys Trp Gly Thr Asp Glu Glu Lys
            180                 185                 190

ttt atc acc atc ttt gga aca cga agt gtg tct cat ttg aga aag gtg        624
Phe Ile Thr Ile Phe Gly Thr Arg Ser Val Ser His Leu Arg Lys Val
            195                 200                 205

ttt gac aag tac atg act ata tca gga ttt caa att gag gaa acc att        672
Phe Asp Lys Tyr Met Thr Ile Ser Gly Phe Gln Ile Glu Glu Thr Ile
            210                 215                 220

gac cgc gag act tct ggc aat tta gag caa cta ctc ctt gct gtt gtg        720
Asp Arg Glu Thr Ser Gly Asn Leu Glu Gln Leu Leu Leu Ala Val Val
225                 230                 235                 240

aaa tct att cga agt ata cct gcc tac ctt gca gag acc ctc tat tat        768
Lys Ser Ile Arg Ser Ile Pro Ala Tyr Leu Ala Glu Thr Leu Tyr Tyr
                245                 250                 255

gct atg aag gga gct ggg aca gat gat cat acc ctc atc aga gtc atg        816

Ala Met Lys Gly Ala Gly Thr Asp Asp His Thr Leu Ile Arg Val Met
            260                 265                 270

gtt tcc agg agt gag att gat ctg ttt aac atc agg aag gag ttt agg        864
Val Ser Arg Ser Glu Ile Asp Leu Phe Asn Ile Arg Lys Glu Phe Arg
            275                 280                 285

aag aat ttt gcc acc tct ctt tat tcc atg att aag gga gat aca tct        912
Lys Asn Phe Ala Thr Ser Leu Tyr Ser Met Ile Lys Gly Asp Thr Ser
            290                 295                 300

ggg gac tat aag aaa gct ctt ctg ctg ctc tgt gga gaa gat gac           957
Gly Asp Tyr Lys Lys Ala Leu Leu Leu Leu Cys Gly Glu Asp Asp
305                 310                 315


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            20                  25                  30


Asp Glu Glu Ser Ile Leu Thr Leu Leu Thr Ser Arg Ser Asn Ala Gln
            35                  40                  45
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3

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Arg Gln Glu Ile Ser Ala Ala Phe Lys Thr Leu Phe Gly Arg Asp Leu
    50              55                  60

Leu Asp Asp Leu Lys Ser Glu Leu Thr Gly Lys Phe Glu Lys Leu Ile
65              70                  75                      80

Val Ala Leu Met Lys Pro Ser Arg Leu Tyr Asp Ala Tyr Glu Leu Lys
            85                  90                  95

His Ala Leu Lys Gly Ala Gly Thr Asn Glu Lys Val Leu Thr Glu Ile
            100             105                 110

Ile Ala Ser Arg Thr Pro Glu Glu Leu Arg Ala Ile Lys Gln Val Tyr
            115             120                 125

Glu Glu Glu Tyr Gly Ser Ser Leu Glu Asp Asp Val Val Gly Asp Thr
    130                 135                 140

Ser Gly Tyr Tyr Gln Arg Met Leu Val Val Leu Leu Gln Ala Asn Arg
145                 150                 155                 160

Asp Pro Asp Ala Gly Ile Asp Glu Ala Gln Val Glu Gln Asp Ala Gln
            165                 170                 175

Ala Leu Phe Gln Ala Gly Glu Leu Lys Trp Gly Thr Asp Glu Glu Lys
            180                 185                 190

Phe Ile Thr Ile Phe Gly Thr Arg Ser Val Ser His Leu Arg Lys Val
    195                 200                 205

Phe Asp Lys Tyr Met Thr Ile Ser Gly Phe Gln Ile Glu Glu Thr Ile
    210                 215                 220

Asp Arg Glu Thr Ser Gly Asn Leu Glu Gln Leu Leu Leu Ala Val Val
225                 230                 235                 240

Lys Ser Ile Arg Ser Ile Pro Ala Tyr Leu Ala Glu Thr Leu Tyr Tyr
            245                 250                 255

Ala Met Lys Gly Ala Gly Thr Asp Asp His Thr Leu Ile Arg Val Met
            260                 265                 270
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Val Ser Arg Ser Glu Ile Asp Leu Phe Asn Ile Arg Lys Glu Phe Arg
        275   280   285

Lys Asn Phe Ala Thr Ser Leu Tyr Ser Met Ile Lys Gly Asp Thr Ser
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gtgaccgact tctccggctt cgacggccgc gccgacgccg aggtgctgcg caaggccatg   120

aagggcctgg gcaccgacga ggactccatc ctgaacctgc tgaccgcccg ctccaacgcc   180

cagcgccagc agatcgccga ggagttcaag accctgttcg ccgcgacct ggtgaacgac   240

atgaagtccg agctgaccgg caagttcgag aagctgatcg tggccctgat gaagccctcc   300

cgcctgtacg acgcctacga gctgaagcac gccaagctgg gcgccggcac cgacgagaag   360

gtgctgaccg agatcatcgc ctcccgcacc cccgaggagc tgcgcgccat caagcaggcc   420

tacgaggagg agtacggctc caacctggag gacgacgtgg tgggcgacac ctccggctac   480

taccagcgca tgctggtggt gctgctgcag gccaaccgcg accccgacac cgccatcgac   540

gacgcccagg tggagctgga cgcccaggcc ctgttccagg ccggcgagct gaagtggggc   600

5

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accgacgagg agaagttcat caccatcctg ggcacccgct ccgtgtccca cctgcgccgc      660

gtgttcgaca agtacatgac catctccggc ttccagatcg aggagaccat cgaccgcgag      720

acctccggca acctggagaa cctgctgctg gccgtggtga agtccatccg ctccatcccc      780

gcctacctgg ccgagaccct gtactacgcc atgaagggcg ccggcaccga cgaccacacc      840

ctgatccgcg tgatcgtgtc ccgctccgag atcgacctgt tcaacatccg caaggagttc      900

cgcaagaact tcgccacctc cctgtactcc atgatcaagg gcgacacctc cggcgactac      960

aagaaggccc tgctgctgct gtgcggcggc gaggacgacn nnagatctcg atcgggcctg     1020

gaggtgctgt tccagggccc cggaagtact nnngccctgc gcggcaccgt gaccgacttc     1080

tccggcttcg acggccgcgc cgacgccgag gtgctgcgca aggccatgaa gggcctgggc     1140

accgacgagg actccatcct gaacctgctg accgcccgct ccaacgccca gcgccagcag     1200

atcgccgagg agttcaagac cctgttcggc cgcgacctgg tgaacgacat gaagtccgag     1260

ctgaccggca agttcgagaa gctgatcgtg gccctgatga gccctcccg cctgtacgac      1320

gcctacgagc tgaagcacgc caagctgggc gccggcaccg acgagaaggt gctgaccgag     1380

atcatcgcct cccgcacccc cgaggagctg cgcgccatca gcaggccta cgaggaggag      1440

tacggctcca acctggagga cgacgtggtg ggcgacacct ccggctacta ccagcgcatg     1500

ctggtggtgc tgctgcaggc caaccgcgac cccgacaccg ccatcgacga cgcccaggtg     1560

gagctggacg cccaggccct gttccaggcc ggcgagctga agtggggcac cgacgaggag     1620

aagttcatca ccatcctggg cacccgctcc gtgtcccacc tgcgccgcgt gttcgacaag     1680

tacatgacca tctccggctt ccagatcgag gagaccatcg accgcgagac ctccggcaac     1740

ctggagaacc tgctgctggc cgtggtgaag tccatccgct ccatccccgc ctacctggcc     1800

gagaccctgt actacgccat gaagggcgcc ggcaccgacg accacaccct gatccgcgtg     1860

atcgtgtccc gctccgagat cgacctgttc aacatccgca aggagttccg caagaacttc     1920

gccacctccc tgtactccat gatcaagggc gacacctccg cgactacaa gaaggccctg     1980

ctgctgctgt gcggcggcga ggacgactaa taataa                                2016
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<212> DNA
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Met Asp Tyr Lys Asp Asp Asp Asp Lys Leu Ala Ala Ala Asn Xaa Ala
1               5                   10                  15

ctg cgc ggc acc gtg acc gac ttc tcc ggc ttc gac ggc cgc gcc gac        96
Leu Arg Gly Thr Val Thr Asp Phe Ser Gly Phe Asp Gly Arg Ala Asp
            20                  25                  30

gcc gag gtg ctg cgc aag gcc atg aag ggc ctg ggc acc gac gag gac       144
Ala Glu Val Leu Arg Lys Ala Met Lys Gly Leu Gly Thr Asp Glu Asp
        35                  40                  45

tcc atc ctg aac ctg ctg acc gcc cgc tcc aac gcc cag cgc cag cag       192
Ser Ile Leu Asn Leu Leu Thr Ala Arg Ser Asn Ala Gln Arg Gln Gln
    50                  55                  60

atc gcc gag gag ttc aag acc ctg ttc ggc cgc gac ctg gtg aac gac       240
Ile Ala Glu Glu Phe Lys Thr Leu Phe Gly Arg Asp Leu Val Asn Asp
65                  70                  75                  80

atg aag tcc gag ctg acc ggc aag ttc gag aag ctg atc gtg gcc ctg       288
Met Lys Ser Glu Leu Thr Gly Lys Phe Glu Lys Leu Ile Val Ala Leu
                85                  90                  95

atg aag ccc tcc cgc ctg tac gac gcc tac gag ctg aag cac gcc aag       336
Met Lys Pro Ser Arg Leu Tyr Asp Ala Tyr Glu Leu Lys His Ala Lys
                100                 105                 110

ctg ggc gcc ggc acc gac gag aag gtg ctg acc gag atc atc gcc tcc       384
Leu Gly Ala Gly Thr Asp Glu Lys Val Leu Thr Glu Ile Ile Ala Ser
            115                 120                 125

cgc acc ccc gag gag ctg cgc gcc atc aag cag gcc tac gag gag gag       432
Arg Thr Pro Glu Glu Leu Arg Ala Ile Lys Gln Ala Tyr Glu Glu Glu
        130                 135                 140
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7

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tac ggc tcc aac ctg gag gac gac gtg gtg ggc gac acc tcc ggc tac        480
Tyr Gly Ser Asn Leu Glu Asp Asp Val Val Gly Asp Thr Ser Gly Tyr
145                 150                 155                 160

tac cag cgc atg ctg gtg gtg ctg ctg cag gcc aac cgc gac ccc gac        528
Tyr Gln Arg Met Leu Val Val Leu Leu Gln Ala Asn Arg Asp Pro Asp
                165                 170                 175

acc gcc atc gac gac gcc cag gtg gag ctg gac gcc cag gcc ctg ttc        576
Thr Ala Ile Asp Asp Ala Gln Val Glu Leu Asp Ala Gln Ala Leu Phe
                180                 185                 190

cag gcc ggc gag ctg aag tgg ggc acc gac gag gag aag ttc atc acc        624
Gln Ala Gly Glu Leu Lys Trp Gly Thr Asp Glu Glu Lys Phe Ile Thr
                195                 200                 205

atc ctg ggc acc cgc tcc gtg tcc cac ctg cgc cgc gtg ttc gac aag        672
Ile Leu Gly Thr Arg Ser Val Ser His Leu Arg Arg Val Phe Asp Lys
                210                 215                 220

tac atg acc atc tcc ggc ttc cag atc gag gag acc atc gac cgc gag        720
Tyr Met Thr Ile Ser Gly Phe Gln Ile Glu Glu Thr Ile Asp Arg Glu
225                 230                 235                 240

acc tcc ggc aac ctg gag aac ctg ctg ctg gcc gtg gtg aag tcc atc        768
Thr Ser Gly Asn Leu Glu Asn Leu Leu Leu Ala Val Val Lys Ser Ile
                245                 250                 255

cgc tcc atc ccc gcc tac ctg gcc gag acc ctg tac tac gcc atg aag        816
Arg Ser Ile Pro Ala Tyr Leu Ala Glu Thr Leu Tyr Tyr Ala Met Lys
                260                 265                 270

ggc gcc ggc acc gac gac cac acc ctg atc cgc gtg atc gtg tcc cgc        864
Gly Ala Gly Thr Asp Asp His Thr Leu Ile Arg Val Ile Val Ser Arg
                275                 280                 285

tcc gag atc gac ctg ttc aac atc cgc aag gag ttc cgc aag aac ttc        912
Ser Glu Ile Asp Leu Phe Asn Ile Arg Lys Glu Phe Arg Lys Asn Phe
    290                 295                 300

gcc acc tcc ctg tac tcc atg atc aag ggc gac acc tcc ggc gac tac        960
Ala Thr Ser Leu Tyr Ser Met Ile Lys Gly Asp Thr Ser Gly Asp Tyr
305                 310                 315                 320

aag aag gcc ctg ctg ctg ctg tgc ggc ggc gag gac gac nnn aga tct       1008
Lys Lys Ala Leu Leu Leu Leu Cys Gly Gly Glu Asp Asp Xaa Arg Ser
                325                 330                 335

cga tcg ggc ctg gag gtg ctg ttc cag ggc ccc gga agt act nnn gcc       1056
Arg Ser Gly Leu Glu Val Leu Phe Gln Gly Pro Gly Ser Thr Xaa Ala
                340                 345                 350

ctg cgc ggc acc gtg acc gac ttc tcc ggc ttc gac ggc cgc gcc gac       1104
Leu Arg Gly Thr Val Thr Asp Phe Ser Gly Phe Asp Gly Arg Ala Asp
                355                 360                 365

gcc gag gtg ctg cgc aag gcc atg aag ggc ctg ggc acc gac gag gac       1152
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8

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Ala Glu Val Leu Arg Lys Ala Met Lys Gly Leu Gly Thr Asp Glu Asp
    370                 375                 380

tcc atc ctg aac ctg ctg acc gcc cgc tcc aac gcc cag cgc cag cag    1200
Ser Ile Leu Asn Leu Leu Thr Ala Arg Ser Asn Ala Gln Arg Gln Gln
385                 390                 395                 400

atc gcc gag gag ttc aag acc ctg ttc ggc cgc gac ctg gtg aac gac    1248
Ile Ala Glu Glu Phe Lys Thr Leu Phe Gly Arg Asp Leu Val Asn Asp
                405                 410                 415

atg aag tcc gag ctg acc ggc aag ttc gag aag ctg atc gtg gcc ctg    1296
Met Lys Ser Glu Leu Thr Gly Lys Phe Glu Lys Leu Ile Val Ala Leu
                420                 425                 430

atg aag ccc tcc cgc ctg tac gac gcc tac gag ctg aag cac gcc aag    1344
Met Lys Pro Ser Arg Leu Tyr Asp Ala Tyr Glu Leu Lys His Ala Lys
            435                 440                 445

ctg ggc gcc ggc acc gac gag aag gtg ctg acc gag atc atc gcc tcc    1392
Leu Gly Ala Gly Thr Asp Glu Lys Val Leu Thr Glu Ile Ile Ala Ser
        450                 455                 460

cgc acc ccc gag gag ctg cgc gcc atc aag cag gcc tac gag gag gag    1440
Arg Thr Pro Glu Glu Leu Arg Ala Ile Lys Gln Ala Tyr Glu Glu Glu
465                 470                 475                 480

tac ggc tcc aac ctg gag gac gac gtg gtg ggc gac acc tcc ggc tac    1488
Tyr Gly Ser Asn Leu Glu Asp Asp Val Val Gly Asp Thr Ser Gly Tyr
                485                 490                 495

tac cag cgc atg ctg gtg gtg ctg ctg cag gcc aac cgc gac ccc gac    1536
Tyr Gln Arg Met Leu Val Val Leu Leu Gln Ala Asn Arg Asp Pro Asp
                500                 505                 510

acc gcc atc gac gac gcc cag gtg gag ctg gac gcc cag gcc ctg ttc    1584
Thr Ala Ile Asp Asp Ala Gln Val Glu Leu Asp Ala Gln Ala Leu Phe
            515                 520                 525

cag gcc ggc gag ctg aag tgg ggc acc gac gag gag aag ttc atc acc    1632
Gln Ala Gly Glu Leu Lys Trp Gly Thr Asp Glu Glu Lys Phe Ile Thr
        530                 535                 540

atc ctg ggc acc cgc tcc gtg tcc cac ctg cgc cgc gtg ttc gac aag    1680
Ile Leu Gly Thr Arg Ser Val Ser His Leu Arg Arg Val Phe Asp Lys
545                 550                 555                 560

tac atg acc atc tcc ggc ttc cag atc gag gag acc atc gac cgc gag    1728
Tyr Met Thr Ile Ser Gly Phe Gln Ile Glu Glu Thr Ile Asp Arg Glu
                565                 570                 575

acc tcc ggc aac ctg gag aac ctg ctg ctg gcc gtg gtg aag tcc atc    1776
Thr Ser Gly Asn Leu Glu Asn Leu Leu Leu Ala Val Val Lys Ser Ile
                580                 585                 590

cgc tcc atc ccc gcc tac ctg gcc gag acc ctg tac tac gcc atg aag    1824
Arg Ser Ile Pro Ala Tyr Leu Ala Glu Thr Leu Tyr Tyr Ala Met Lys
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9

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                595                     600                     605

ggc gcc ggc acc gac gac cac acc ctg atc cgc gtg atc gtg tcc cgc        1872
Gly Ala Gly Thr Asp Asp His Thr Leu Ile Arg Val Ile Val Ser Arg
    610                     615                     620

tcc gag atc gac ctg ttc aac atc cgc aag gag ttc cgc aag aac ttc        1920
Ser Glu Ile Asp Leu Phe Asn Ile Arg Lys Glu Phe Arg Lys Asn Phe
625                     630                     635                     640

gcc acc tcc ctg tac tcc atg atc aag ggc gac acc tcc ggc gac tac        1968
Ala Thr Ser Leu Tyr Ser Met Ile Lys Gly Asp Thr Ser Gly Asp Tyr
                    645                     650                     655

aag aag gcc ctg ctg ctg ctg tgc ggc ggc gag gac gac taa taa taa        2016
Lys Lys Ala Leu Leu Leu Leu Cys Gly Gly Glu Asp Asp
                660                     665
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<220>
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<223>  The 'Xaa' at location 334 stands for Lys, Asn, Arg, Ser, Thr,
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       Cys, or Phe.

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<223>  The 'Xaa' at location 351 stands for Lys, Asn, Arg, Ser, Thr,
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       Cys, or Phe.

<220>
<223>  primer

<400>  6
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Met Asp Tyr Lys Asp Asp Asp Asp Lys Leu Ala Ala Ala Asn Xaa Ala
1                   5                   10                  15


Leu Arg Gly Thr Val Thr Asp Phe Ser Gly Phe Asp Gly Arg Ala Asp
                20                  25                  30


Ala Glu Val Leu Arg Lys Ala Met Lys Gly Leu Gly Thr Asp Glu Asp
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10

Ser Ile Leu Asn Leu Leu Thr Ala Arg Ser Asn Ala Gln Arg Gln Gln
    50   55   60

Ile Ala Glu Glu Phe Lys Thr Leu Phe Gly Arg Asp Leu Val Asn Asp
65   70   75   80

Met Lys Ser Glu Leu Thr Gly Lys Phe Glu Lys Leu Ile Val Ala Leu
                85   90   95

Met Lys Pro Ser Arg Leu Tyr Asp Ala Tyr Glu Leu Lys His Ala Lys
            100   105   110

Leu Gly Ala Gly Thr Asp Glu Lys Val Leu Thr Glu Ile Ile Ala Ser
        115   120   125

Arg Thr Pro Glu Glu Leu Arg Ala Ile Lys Gln Ala Tyr Glu Glu Glu
    130   135   140

Tyr Gly Ser Asn Leu Glu Asp Asp Val Val Gly Asp Thr Ser Gly Tyr
145   150   155   160

Tyr Gln Arg Met Leu Val Val Leu Leu Gln Ala Asn Arg Asp Pro Asp
            165   170   175

Thr Ala Ile Asp Asp Ala Gln Val Glu Leu Asp Ala Gln Ala Leu Phe
            180   185   190

Gln Ala Gly Glu Leu Lys Trp Gly Thr Asp Glu Glu Lys Phe Ile Thr
        195   200   205

Ile Leu Gly Thr Arg Ser Val Ser His Leu Arg Arg Val Phe Asp Lys
    210   215   220

Tyr Met Thr Ile Ser Gly Phe Gln Ile Glu Glu Thr Ile Asp Arg Glu
225   230   235   240

Thr Ser Gly Asn Leu Glu Asn Leu Leu Leu Ala Val Val Lys Ser Ile
            245   250   255

Arg Ser Ile Pro Ala Tyr Leu Ala Glu Thr Leu Tyr Tyr Ala Met Lys
            260   265   270

11

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Gly Ala Gly Thr Asp Asp His Thr Leu Ile Arg Val Ile Val Ser Arg
        275             280             285

Ser Glu Ile Asp Leu Phe Asn Ile Arg Lys Glu Phe Arg Lys Asn Phe

    290                 295                 300

Ala Thr Ser Leu Tyr Ser Met Ile Lys Gly Asp Thr Ser Gly Asp Tyr
305                 310             315                 320

Lys Lys Ala Leu Leu Leu Leu Cys Gly Gly Glu Asp Asp Xaa Arg Ser
            325             330                 335

Arg Ser Gly Leu Glu Val Leu Phe Gln Gly Pro Gly Ser Thr Xaa Ala
            340             345             350

Leu Arg Gly Thr Val Thr Asp Phe Ser Gly Phe Asp Gly Arg Ala Asp
            355             360             365

Ala Glu Val Leu Arg Lys Ala Met Lys Gly Leu Gly Thr Asp Glu Asp
        370             375             380

Ser Ile Leu Asn Leu Leu Thr Ala Arg Ser Asn Ala Gln Arg Gln Gln
385             390             395                 400

Ile Ala Glu Glu Phe Lys Thr Leu Phe Gly Arg Asp Leu Val Asn Asp
            405             410                 415

Met Lys Ser Glu Leu Thr Gly Lys Phe Glu Lys Leu Ile Val Ala Leu
            420             425             430

Met Lys Pro Ser Arg Leu Tyr Asp Ala Tyr Glu Leu Lys His Ala Lys
            435             440             445

Leu Gly Ala Gly Thr Asp Glu Lys Val Leu Thr Glu Ile Ile Ala Ser
        450             455             460

Arg Thr Pro Glu Glu Leu Arg Ala Ile Lys Gln Ala Tyr Glu Glu Glu
465             470             475                 480

Tyr Gly Ser Asn Leu Glu Asp Asp Val Val Gly Asp Thr Ser Gly Tyr
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Tyr Gln Arg Met Leu Val Val Leu Leu Gln Ala Asn Arg Asp Pro Asp
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Thr Ala Ile Asp Asp Ala Gln Val Glu Leu Asp Ala Gln Ala Leu Phe
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Gln Ala Gly Glu Leu Lys Trp Gly Thr Asp Glu Glu Lys Phe Ile Thr
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Ile Leu Gly Thr Arg Ser Val Ser His Leu Arg Arg Val Phe Asp Lys
545              550              555              560

Tyr Met Thr Ile Ser Gly Phe Gln Ile Glu Glu Thr Ile Asp Arg Glu
          565              570              575

Thr Ser Gly Asn Leu Glu Asn Leu Leu Leu Ala Val Val Lys Ser Ile
          580              585              590

Arg Ser Ile Pro Ala Tyr Leu Ala Glu Thr Leu Tyr Tyr Ala Met Lys
          595              600              605

Gly Ala Gly Thr Asp Asp His Thr Leu Ile Arg Val Ile Val Ser Arg
          610              615              620

Ser Glu Ile Asp Leu Phe Asn Ile Arg Lys Glu Phe Arg Lys Asn Phe
625              630              635              640

Ala Thr Ser Leu Tyr Ser Met Ile Lys Gly Asp Thr Ser Gly Asp Tyr
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Lys Lys Ala Leu Leu Leu Leu Cys Gly Gly Glu Asp Asp
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